DATA AND SAFETY MONITORING BOARDS

Larry Friedman, M.D.

A. Purposes of Monitoring

1. Participant Safety

2. Study Integrity

3. Public Health

B. What? Who?

1. The Data and Safety Monitoring Board (DSMB) should be independent of the investigators and sponsor

a. It should be appointed by?

b. It should report to?

c. Definition of "independent"

d. Issue of conflict of interest

2. Members should have expertise in relevant disciplines

a. Scientific area

b. Trial design / biostatistics

c. ? Ethics, ? Patient representative / advocate

3. Possible attendance by representatives of

   a. sponsor

   b. industry

   c. FDA

   (depends on phase of study and what data are being presented)

C. How?

1. Monitoring should be done on

   a. Participant enrollment

   b. Protocol compliance

   c. Data quality

   d. Baseline variables (group balance, kinds of participants)

   e. Interim variables

   f. Response variables

      i. Primary outcome

      ii. Secondary outcomes

      iii. Adverse events

2. Frequency of Monitoring Depends on

a. Duration of study

b. Rapidity of data accumulation

D. Issues in Data Monitoring

1. One-Sided vs 2-Sided Test, Asymmetric Boundaries

2. Use of External Information, Cumulative Meta-Analysis

3. Repeated Testing for Significance

4. Who Should Know Accumulating Data? What? When?

E. Monitoring Techniques for Primary Response Variables

1. Classical Sequential

2. Group Sequential

3. Curtailed Sampling

F. Decision Making

1. Reasons for Early Stopping

a. Has the intervention been proven to be beneficial?

b. Has the intervention been shown to be harmful?

c. Is there a realistic chance of detecting a significant or meaningful difference if the study were to continue to its scheduled end?

2. Possible Reasons for Extending

    a. Low power

        i. inadequate numbers

        ii. low event rate

    b. Strong (nonsignificant) trend

    c. To answer secondary questions

3. Change Protocol

    a. Drop an arm

    b. Drop participant subset

    c. Change entry criteria

4. Proceed As Planned

G. Examples of DSMB Decisions